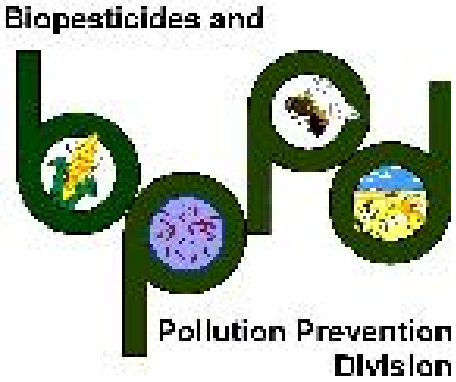

BIOCHEMICAL PESTICIDES: INFORMATION TO SUPPORT SUCCESSFUL WAIVER REQUESTS AND GUIDELINE-BY-GUIDELINE EXAMPLES

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DRAFT ONLY

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OVERVIEW

The data requirements for biochemical pesticides are specified in the data tables listed under 40 CFR 158.690 (a) through (d). [*Note: When theBiochemical Pesticides Data Requirements Table updates are published, the data tables will be found under 40 CFR 158.2030 through 158.2084 (proposed)]*

I. All appropriate data requirements MUST be fulfilled for technical grade active ingredients (TGAIs), Manufacturing-use Products (MPs), and End-use Products (EPs).

II. Data requirements may be fulfilled with Guideline studies or with waiver requests. Protocols for Guideline studies may be accessed online at: http://www.epa.gov/opptsfrs/home/guidelin.htm

Series 830 Product Chemistry
Seires 870 Health Effects
Series 850 Ecological Effects (Non-target Organisms)
Series 860 Residue Chemistry (required only if tolerances must be established)

III. A waiver request is a request for a waiver from the requirement to conduct a Guideline study. A waiver request DOES NOT provide an exemption from need to fulfill/address a particular data requirement. Therefore, there are no waivers from any data requirement (except as specified in IV below).

IV. Certain data requirements may be inappropriate due to unusual physical, chemical, and/or biological properties, or atypical use patterns of a particular product, that would make it difficult to conduct a study or would not provide the Agency with information that would be useful in conducting a risk assessment. However, sufficient data must be available to support applicable statutory standards. [see 40 CFR 158.45 (a)(1)]

V. *"The Agency will waive data requirements"* (i.e. the requirement to conduct a Guideline study) *"on a case-by-case basis in response to written requests by the registrant"* [40 CFR 158.45 (a)(2)].

VI.A. For Product Chemistry data [40 CFR 158.690(a) and 40 CFR 158.190] data requirements are either applicable or not applicable for a particular product (TGAI, MP, EP) and/or formulation type (liquid, powder, granule, etc.). All applicable data requirements must be satisfied.

VI.B. When the TGAI is a Food Grade substance, and the Food Grade status has been verified through documentation as provided by the supplier, the following data requirements need not be fulfilled:

Manufacturing Process
Five-Batch Analysis
Analytical Methods

VII. All toxicology [Health Effects; 40 CFR 158.690(c)] waiver requests must contain specific, quantitative data and/or information (as appropriate for a particular data requirement) regarding acute, subchronic, and/or chronic toxicity and/or irritation, genotoxicity, immune response, and/or teratogenicity of the biochemical pesticide. Toxicity data submitted in support of a particular waiver request must be equivalent to the data that would have been obtained from a Guideline study. Alternatively, data/information must **unequivocally** demonstrate a lack of toxicity by the route of exposure (e.g. oral, dermal, inhalation, etc.) for which the waiver is requested and/or a lack of exposure to the pesticide when it is used according to proposed label use rates, timing and sites.

VIII. All data for non-target organism [Ecological Effects;40 CFR 158.690(d)] waiver requests must contain specific, quantitative data and/or information (as appropriate for a particular data requirement) regarding the toxicity of a biochemical pesticide to non-target birds, fish and aquatic invertebrates, insects, and plants via intentional and unintentional (e.g. spray drift, runoff, etc.) exposure. Ecotoxicity data submitted in support of a particular waiver request must be equivalent to the data that would have been obtained from a Guideline study. Alternatively, data/information must unequivocally demonstrate a lack of toxicity to the exposed taxa and/or a lack of exposure of non-target taxa to the pesticide when it is used according to proposed label use rates, timing and sites.

IX. For any quantitative data obtained from non-guideline studies (e.g. published technical literature) that are used to support a waiver request, a complete reference citation and/or a list of references (if more than one is cited), as well as a copy of the reference (or the pertinent portion or the reference if it is unusually large), including the methodology used, must be submitted.

X. Tabularize data to support any text discussions, particularly in any comprehensive data summaries (for multiple toxicity pathways and multiple non-target taxa) that would precede the discussion of individual waiver requests (see tabular examples below).

EXAMPLE SUMMARY TABLE FOR TIER I TOXICITY

Table X. Tier I Toxicity Profile for [*TGAI or MP or EP*] [1, 2]

Study Type/OPPTS Guideline	**LD_{50}/LC_{50}/Results**	**Toxicity Category** [3]	**MRID** [4]
Acute Oral Toxicity/OPPTS 870.1100 [5]	mg/kg	I, II, III, or IV	
Acute Dermal Toxicity/OPPTS 870.1200 [5]	mg/kg	I, II, III, or IV	
Acute Inhalation Toxicity/OPPTS 870.1300 [5]	mg/L	I, II, III, or IV	
Acute Eye Irritation/OPPTS 870.2400 [5]	Briefly describe symptoms & duration	I, II, III, or IV	
Acute Dermal Irritation/OPPTS 870.2500 [5]	Briefly describe symptoms & duration	I, II, III, or IV	
Skin Sensitization/OPPTS 870.2600 [5]	Briefly describe results	sensitizer/not a sensitzer	
Genotoxicity/OPPTS 870.5265	same as above	mutagen/not a mutagen	
OPPTS 870.5300	same as above		
OPPTS 870.5395	same as above		
Immune Response/OPPTS 870.7800	same as above	immunotoxic/not immunotoxic	
90-Day Feeding/OPPTS 870.3100	mg/kg/day for x days	toxicity/no toxicity	
90-Day Dermal/OPPTS 870.3250	mg/kg/day for x days	toxicity/no toxicity	
90-Day Inhalation/OPPTS 870.3465	mg/L/day for x days	toxicity/no toxicity	
Teratogenicity/OPPTS 870.3500	Briefly describe results	teratogenic/not teratogenic	

[1] Add footnotes as necessary

[2] Only tabularize the data requirements that are appropriate for a particular product (e.g. TGAI, MP, or EP); see Tables under 40 CFR 158.690 to determine which data requirements are applicable.

[3] When applicable

[4] Or other citation, when applicable

[5] For EPs with registered TGAIs; EPs with non-registered TGAIs must fulfill all Tier I Toxicity data requirements

EXAMPLE SUMMARY TABLE FOR TIER I NON-TARGET ORGANISMS

Table X. Non-Target Organism Toxicity Profile for [*TGAI*] [1, 2]

Study Type/OPPTS Guideline	**LD_{50}/LC_{50}/Results**	**Toxicity Category** [3]	**MRID** [4]
Avian Acute Oral/OPPTS 850.2100	mg/kg		
Avian Dietary/OPPTS 850.2200	mg/kg		
Freshwater Fish LC50/OPPTS 850.1075	mg/L		
Freshwater Invertebrate/OPPTS 850.1010	mg/L		
Non-target Plants/OPPTS 850.4025 [5] OPPTS 850.4100 OPPTS 850.4150 OPPTS 850.4200 OPPTS 850.4230 OPPTS 850.4400	Footnote 6		
Non-target Insects/OPPTS 850.3020 OPPTS 850.3030 OPPTS 850.3040	ug/kg		

[1] Add footnotes as necessary

[2] Only tabularize the data requirements that are appropriate for a particular product; see Tables under 40 CFR 158.690 to determine which data requirements are applicable.

[3] Practically non-toxic, slightly toxic, moderately toxic, highly toxic, or very highly toxic as applicable

[4] Or other citation when applicable

[5] Provide data/information only for those Guideline requirements that are appropriate for the product type, use site(s), and exposure scenarios

[6] Describe treatment rate at which 25% or more injury ocurrred (if data are available, or other effect if applicable).

SAMPLE WAIVER REQUEST FORMAT FOR BIOCHEMICAL PESTICIDE TOXICITY DATA REQUIREMENTS

To determine that a waiver request conforms to the guidance listed in the Overview, the following information must be submitted on a Guideline-by-Guideline basis:

STUDY TYPES: **Tier I:**
[see also Acute Toxicity Testing – Background (OPPTS 870.1000; December 2002 revision)]

I. Acute Oral (Limit Test) Toxicity (OPPTS 870.1100; December 2002 revision) or Acute Oral Toxicity: Up-and-Down Procedure (OECD 425)

ACTIVE INGREDIENT:

SYNONYMS:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct an Acute Oral Toxicity study (OPPTS 870.1100 or OECD 425). The waiver request is based on the rationale that (one or more of the following):

a. [*active ingredient name*] is a naturally-occurring substance [*describe source*], whose level in the environment will not significantly increase above background levels and/or will rapidly degrade when [*product name*] is used in accordance with proposed label use directions. AND/OR

b. An extensive literature search yielded no reports of toxicity or other adverse effects in [*humans, rodents, other mammals, etc*] by the oral route of exposure. AND/OR

c. An extensive literature search demonstrated that acute oral toxicity and/or mortality and/or adverse effects occurred at doses >5000 mg/kg (Tox IV) [*give species, LD_{50} and literature citation*] AND/OR

d. The proposed uses of [*product name*] on [*use sites/crops*] will not result in any exposure or adverse effects to humans via the oral route of exposure [BRIEFLY d*iscuss how/why*]. Therefore, testing is not considered necessary to assess the acute oral toxicity of [*active ingredient name*]. AND/OR

e. The product/[*active ingredient name*] is a gas or is highly volatile or is contained within a trap or closed dispenser that precludes oral ingestion by workers, applicators, and/or the public.

f. The product is corrosive or has a pH <2.0 or >11.5, which precludes testing on experimental animals; it will be classified in Toxicity Category I on the basis of

potential injury via the oral route of exposure..

WAIVER REQUEST JUSTIFICATION:
The waiver request for acute oral toxicity is based on [*one or more of*] the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe levels of naturally-occurring substance in environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Describe environmental fate and/or degradation rate and/or formation of metabolites and metabolite fate/degradation (*). AND/OR

No evidence of oral toxicity and/or low oral toxicity and/or no adverse effects: A literature search of the [*e.g. TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year range*] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the search words, to ascertain whether there were any acute oral toxicity data on humans and/or other mammals. There [*are/are no*] acute toxicity data available demonstrating that there are [*toxic effects/no toxic effects*] by the oral route of exposure to naturally-occurring sources of [*active ingredient name*] (*) [*NOTE: If toxic effects have been reported, give LD_{50} and literature citation(s)*]

Proposed label uses mitigate/eliminate oral exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating direct oral exposure to humans, AND/OR timing of application precludes direct/indirect oral exposure to humans [*Discuss proposed label use sites and rate/timing of application, application methods, and their effects on limiting oral exposure, if applicable*] (*).

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph IX for further guidance)

I. Acute Dermal Toxicity (OPPTS 870.1200)

ACTIVE INGREDIENT:

SYNONYMS:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct an Acute Dermal Toxicity study (OPPTS 870.1200). The waiver request is based on

the rationale that (one or more of the following):

a. [*active ingredient name*] is a naturally-occurring substance [*describe source*], whose level in the environment will not significantly increase above background levels and/or will rapidly degrade when [*product name*] is used in accordance with proposed label use directions. AND/OR

b. An extensive literature search yielded no reports of dermal toxicity or other adverse effects in [*humans, rodents, other mammals, etc*] by the dermal route of exposure. AND/OR

c. An extensive literature search demonstrated that dermal toxicity and/or mortality and/or adverse effects occurred at doses >5000 mg/kg (Tox IV) [*give species, LD_{50} and literature citation*] AND/OR

d. The proposed uses of [*product name*] on [*use sites/crops*] will not result in any exposure or adverse effects to humans via the dermal route of exposure [*Discuss how/why*]. Therefore, testing is not considered necessary to assess the acute dermal toxicity of [*active ingredient name*]. AND/OR

e. The product/[*active ingredient name*] is a gas or is highly volatile or is contained within a trap or closed dispenser that precludes dermal contact by workers, applicators, and/or the public.

f. The product is corrosive or has a pH <2.0 or >11.5, which precludes testing on experimental animals; it will be classified in Toxicity Category I on the basis of potential injury via the dermal route of exposure.

WAIVER REQUEST JUSTIFICATION:

The waiver request for acute dermal toxicity is based on [*one or more of*] the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe levels of naturally-occurring substance in environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Describe environmental fate and/or degradation rate and/or formation of metabolites and metabolite fate/degradation (*). AND/OR

No evidence of dermal toxicity and/or low dermal toxicity and/or no adverse effects: A literature search of the [*e.g. TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year range*] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the

search words, to ascertain whether there were any acute dermal toxicity data on humans and/or other mammals. There [*are/are no*] acute toxicity data available demonstrating that there are [*toxic effects/no toxic effects*] by the dermal route of exposure to naturally-occurring sources of [*active ingredient name*] (*) [*NOTE: If toxic effects have been reported, give LD_{50} and literature citation(s)*]

Proposed label uses mitigate/eliminate exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating direct dermal exposure to humans, AND/OR timing of application precludes direct/indirect dermal exposure to humans [*Discuss proposed label use sites and rate/timing of application, application methods, and their effects on limiting dermal exposure, if applicable*] (*).

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph IX for further guidance)

III. Acute Inhalation Toxicity (OPPTS 870.1300)

ACTIVE INGREDIENT:

SYNONYMS:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct an Acute Inhalation Toxicity study (OPPTS 870.1300). The waiver request is based on the rationale that (one or more of the following):

a. [*active ingredient name*] is a naturally-occurring substance [*describe source*], whose level in the environment will not significantly increase above atmospheric background levels when [*product name*] is used in accordance with proposed label use directions. AND/OR

b. An extensive literature search yielded no reports of toxicity or other adverse effects in [*humans, rodents, other mammals, etc*] by [*active ingredient name*] by the inhalation pathway of exposure. AND/OR

c. An extensive literature search demonstrated that inhalation toxicity and/or mortality and/or adverse effects occurred at doses >2.0 mg/L (Tox IV) [*give LC_{50} and literature citation*] and atmospheric concentrations of [*active ingredient name*] will not exceed this level when [*product name*] is used in accordance with approved labeling. AND/OR

d. The proposed uses of [*product name*] on [*use sites/crops*] will not result in any exposure or adverse effects to humans via the inhalation route exposure [*BRIEFLY discuss how/why*]. Therefore, testing is not considered necessary to assess the acute inhalation toxicity of [*active ingredient name*]. AND/OR

f. The product is corrosive or has a pH <2.0 or >11.5, which precludes testing on experimental animals; it will be classified in Toxicity Category I on the basis of potential injury via the inhalation route of exposure..

WAIVER REQUEST JUSTIFICATION:
The waiver request for acute inhalation toxicity is based on [*one or more of*] the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe atmospheric levels of naturally-occurring substance in environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Describe environmental fate and/or degradation rate and/or formation of metabolites and metabolite fate/degradation (*). AND/OR

No evidence of inhalation toxicity and/or low inhalation toxicity and/or no adverse effects: A literature search of the [*e.g. TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year range*] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the search words, to ascertain whether there were any acute inhalation toxicity data on humans and/or other mammals. There [*are/are no*] acute toxicity data available demonstrating that there are [*toxic effects/no toxic effects*] by the inhalation route of exposure to naturally-occurring sources of [*active ingredient name*] (*) [*NOTE: If toxic effects have been reported, give LC_{50} and literature citation(s)*]

Proposed label uses mitigate/eliminate exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating direct inhalation exposure to humans, AND/OR timing of application precludes direct/indirect inhalation exposure to humans [*Discuss proposed label use sites and rate/timing of application, application methods and its effects on limiting inhalation exposure, if applicable*] (*)

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph IX for further guidance)

IV. Acute Eye Irritation (OPPTS 870.2400)

ACTIVE INGREDIENT:

SYNONYMS:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct an Acute Eye Irritation study (OPPTS 870.2400). The waiver request is based on the rationale that (one or more of the following):

a. An extensive literature search yielded no reports of irritation or other adverse effects in [*humans, rodents, other mammals, etc*] by the ocular pathway of exposure AND/OR

b. An extensive literature search demonstrated that ocular irritation and/or other adverse effects were minimal and reversed in less than 24-hours post-dosing (Tox IV) [also *give time after dosing when no ocular effects were observed and literature citation*] AND/OR

c. The proposed uses of [*product name*] on [*use sites/crops*] will not result in any exposure or adverse effects to humans via the ocular route exposure [*BRIEFLY discuss how/why*]. Therefore, testing is not considered necessary to assess the potential for acute eye irritation by [*active ingredient name*]. AND/OR

d. The product/[*active ingredient name*] is contained within a trap or closed dispenser that precludes ocular exposure to workers, applicators, and/or the public. AND/OR

e. The product is corrosive to the eye or has a pH <2.0 or >11.5, which precludes testing on experimental animals; it will be classified in Toxicity Category I on the basis of potential injurious effects to the eye.

WAIVER REQUEST JUSTIFICATION:
The waiver request for acute eye irritation is based on [*one or more of*] the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe levels of naturally-occurring substance in environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Describe environmental fate and/or degradation rate and/or formation of metabolites and metabolite fate/degradation (*). AND/OR

No evidence of ocular irritation and/or other ocular effects and/or no adverse ocular effects: A literature search of the [*e.g. TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year*

range] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the search words, to ascertain whether there were any acute ocular irritation data on humans and/or other mammals. There [*are/are no*] acute ocular irritation data available demonstrating that there are [*effects/no effects*] by the ocular route of exposure to naturally-occurring sources of [*active ingredient name*] (*) [*NOTE: If adverse ocular effects have been reported, give information regarding severity and duration of effects, and literature citation(s)*]

Proposed label uses mitigate/eliminate exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating direct ocular exposure to humans, AND/OR timing of application precludes direct/indirect ocular exposure to humans [*Discuss proposed label use sites and rate/timing of application, application methods and its effects on limiting dermal exposure*] (*).

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph IX for further guidance)

V. Acute Dermal Irritation (OPPTS 870.2500)

ACTIVE INGREDIENT:

SYNONYMS:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct an Acute Dermal Irritation study (OPPTS 870.2400). The waiver request is based on the rationale that (one or more of the following):

a. An extensive literature search yielded no reports of irritation or other adverse effects in [*humans, rodents, other mammals, etc*] by the dermal pathway of exposure AND/OR

b. An extensive literature search demonstrated that dermal irritation and/or other adverse effects were mild or slight at 72-hours post-dosing (Tox IV) [also *give time after dosing when no dermal effects were observed and literature citation*] AND/OR

d. The proposed uses of [*product name*] on [*use sites/crops*] will not result in any exposure or adverse effects to humans via the dermal route exposure [*Discuss how/why*]. Therefore, testing is not considered necessary to assess the potential for acute dermal irritation by [*active ingredient name*]. AND/OR

e. The [*product* or *active ingredient name*] is contained within a trap or closed dispenser that precludes dermal exposure to workers, applicators, and/or the public. AND/OR

f. The product is corrosive to the skin or has a pH <2.0 or >11.5, which precludes testing on experimental animals; it will be classified in Toxicity Category I on the basis of potential injurious effects to the skin.

WAIVER REQUEST JUSTIFICATION:
The waiver request for acute dermal irritation is based on the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe levels of naturally-occurring substance in environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Describe environmental fate and/or degradation rate and/or formation of metabolites and metabolite fate/degradation (*). AND/OR

No evidence of dermal irritation and/or other dermal effects and/or no adverse ocular effects: A literature search of the [*e.g. TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year range*] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the search words, to ascertain whether there were any acute dermal irritation data on humans and/or other mammals. There [*are/are no*] acute dermal irritation data available demonstrating that there are [*effects/no effects*] by the dermal route of exposure to naturally-occurring sources of [*active ingredient name*] (*) [*NOTE: If dermal effects have been reported, give information regarding severity and duration of effects, and literature citation(s)*](*)

Proposed label uses mitigate/eliminate exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating direct dermal exposure to humans, AND/OR timing of application precludes direct/indirect dermal exposure to humans [*Discuss proposed label use sites and rate/timing of application, application methods and its effects on limiting dermal exposure*] (*).

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph IX for further guidance)

VI. Skin Sensitization (OPPTS 870.2600)

ACTIVE INGREDIENT:

SYNONYMS:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct a Skin Sensitization study (OPPTS 870.2600). The waiver request is based on the rationale that (one or more of the following):

a. The proposed uses of [*product name*] on [*use sites/crops*] will not result in repeated contact with human skin under conditions of use [*Briefly discuss how/why*]. Therefore, testing is not considered necessary to assess the potential for skin sensitization by dermal contact with [*active ingredient name*]. AND/OR

b. An extensive literature search yielded no reports of skin sensitization effects in [*humans, rodents, other mammals, etc*] by the dermal pathway of exposure AND/OR

c. The product/[*active ingredient name*] is contained within a trap or closed dispenser that precludes dermal exposure to workers, applicators, and/or the public. AND/OR

d. The product is corrosive to the skin or has a pH <2.0 or greater than 11.5 which precludes testing on experimental animals; it will be classified in Toxicity Category I on the basis of potential injurious effects to the skin.

WAIVER REQUEST JUSTIFICATION:
The waiver request for skin sensitization studies is based on [*one or more of*] the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe levels of naturally-occurring substance in environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Describe environmental fate and/or degradation rate and/or formation of metabolites and metabolite fate/degradation (*). AND/OR

No evidence of skin sensitization effects: A literature search of the [*e.g. TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year range*] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the search words, to ascertain whether there were any skin sensitization data on humans and/or other mammals. There [*are/are no*] skin sensitization data available demonstrating that there are [*effects/no effects*] by the dermal route of

exposure to naturally-occurring sources of [*active ingredient name*] (*) [*NOTE: If skin sensitization effects have been reported, give information regarding severity and duration of effects, and literature citation(s)*]

Proposed label uses mitigate/eliminate exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating direct/indirect dermal exposure to humans, AND/OR timing of application precludes direct/indirect dermal exposure to humans [*Discuss proposed label use sites and rate/timing of application, application methods and its effects on limiting exposure*] (*).

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph IX for further guidance)

VI. Studies to Detect Genotoxicity
The Salmonella typhimurium Reverse Mutation (Ames) Assay (OPPTS 870.5100)
Detection of Gene Mutations in Somatic Cells in Culture (OPPTS 870.5300)
Mammalian Erythrocyte Micronucleus Test (OPPTS 870.5395)

ACTIVE INGREDIENT:

SYNONYMS:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct Genotoxicity Studies (OPPTS 870.5100; 870.5300; & 870.5395). The waiver request is based on the rationale that (one or more of the following):

a. [*Active ingredient name*] and its metabolites is (are) not structurally related to a known mutagen(s), nor belong(s) to any chemical class of compounds containing known mutagens.

b. An extensive literature search yielded no reports of genotoxic effects in [*humans, rodents, other mammals, etc*] AND/OR

c. [*Active ingredient name*] is ubiquitous in the environment and humans are regularly exposed to this substance via [*describe all routes of exposure*] at levels that are [equal to/greater than] that which would be expected from the product under conditions of use.

d. The proposed uses of [*product name*] on [*use sites/crops*] will not result exposure to humans under conditions of use [*BRIEFLY discuss how/why*]. Therefore, testing is

not considered necessary to assess the potential genotoxicity of [*active ingredient name*]. AND/OR

e. The product containing [a*ctive ingredient name*] is contained within a trap or closed dispenser that precludes any exposure to workers, applicators, and/or the public.

f. The TGAI and/or product is corrosive or has a pH <2.0 or greater than 11.5. The pH is [*too low/too high*] to conduct these studies.

WAIVER REQUEST JUSTIFICATION:

The waiver request for genotoxicity studies is based on [*one or more of*] the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe levels of naturally-occurring substance in environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Describe environmental fate and/or degradation rate and/or formation of metabolites and metabolite fate/degradation (*). AND/OR

No evidence of genotoxic effects: A literature search of the [*e.g. TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year range*] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the search words, to ascertain whether there were any immunotoxicity data on humans and/or other mammals. Is there a long history of exposure to naturally-occurring or anthropogenic sources of [*active ingredient name*] without reported genotoxic effects. (*) There [*are/are no*] genotoxicity data available. [*NOTE: If genotoxic effects have been reported, but do not reflect exposure to the active ingredient under conditions of use, give information regarding the genotoxic effects, the likelihood of their occurrence under conditions of use, and literature citation(s)*] (*)

Proposed label uses mitigate/eliminate exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating direct exposure to humans, AND/OR timing of application precludes direct/indirect exposure to humans [*Discuss proposed label use sites and rate/timing of application, application methods and its effects on limiting exposure*] (*).

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph IX for further guidance)

VII. Immunotoxicity (Immune Response) (OPPTS 870.7800)

ACTIVE INGREDIENT:

SYNONYMS:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct an Immunotoxicity Studies (OPPTS 870.7800). The waiver request is based on the rationale that (one or more of the following):

a. An extensive literature search yielded no reports of immunotoxic effects in [*humans, rodents, other mammals, etc*] AND/OR

b. [*Active ingredient name*] is ubiquitous in the environment and humans are regularly exposed to this substance via [*describe all routes of exposure*] at levels that are [equal to/greater than] that which would be expected from the product under conditions of use.

c. The proposed uses of [*product name*] on [*use sites/crops*] will not result exposure to humans under conditions of use [*Discuss how/why*]. Therefore, testing is not considered necessary to assess the potential immunotoxicity of [*active ingredient name*]. AND/OR

d. The product containing [a*ctive ingredient name*] is contained within a trap or closed dispenser that precludes any exposure to workers, applicators, and/or the public.

e. The TGAI and/or product is corrosive or has a pH <2.0 or >11.5. The pH is [*too low/too high*] to conduct these studies

WAIVER REQUEST JUSTIFICATION:
The waiver request for an immunotoxicity study is based on [*one or more of*] the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe levels of naturally-occurring substance in environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Is there is a long history of human exposure without any reports of immunotoxicological effects (*). AND/OR

No evidence of genotoxic effects: A literature search of the [*e.g. TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year range*] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the search words, to ascertain whether there were

any genotoxicity data on humans and/or other mammals. Is there a long history of exposure to naturally-occurring or anthropogenic sources of [*active ingredient name*] without reported immunotoxic effects. (*) There [*are/are no*] genotoxicity data available. [*NOTE: If genotoxic effects have been reported, but do not reflect exposure to the active ingredient under conditions of use, give information regarding the immunotoxic effects, the likelihood of their occurrence under conditions of use, and literature citation(s)*] (*)

Proposed label uses mitigate/eliminate exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating direct exposure to humans, AND/OR timing of application precludes direct/indirect exposure to humans [*Discuss proposed label use sites and rate/timing of application, application methods and its effects on limiting exposure*] (*).

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph IX for further guidance)

VIII. 90-day Oral Toxicity (90-day Feeding) (OPPTS 870.3100)

ACTIVE INGREDIENT:

SYNONYMS:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct a 90-day Oral Toxicity Study (OPPTS 870.3100). The waiver request is based on the rationale that (one or more of the following):

a. [*Active ingredient name*] does not require a tolerance or an exemption from a requirement of a tolerance, or its use does not require a food additive regulation, or the use of the product is not likely to result in repeated human exposure by the oral route. AND/OR

b. An extensive literature search yielded no reports of subchronic oral toxicity effects in [*humans, rodents, other mammals, etc*] from [*active ingredient name*] AND/OR

c. [*Active ingredient name*] is ubiquitous in the environment and and humans are regularly exposed to this substance orally at levels that are [equal to/greater than] that which would be expected from the product under conditions of use. (*)

d. The proposed uses of [*product name*] on [*use sites/crops*] will not result oral exposure to humans under conditions of use [*Discuss how/why*]. Therefore, testing is not

considered necessary to assess the potential subchronic oral toxicity of [*active ingredient name*]. AND/OR

d. The product containing [a*ctive ingredient name*] is contained within a trap or closed dispenser that precludes any oral exposure to workers, applicators, and/or the public.

e. The TGAI and/or product is corrosive or has a pH <2.0 or >11.5. The pH is [*too low/too high*] to conduct these studies

WAIVER REQUEST JUSTIFICATION:
The waiver request for a 90-day oral toxicity study is based on [*one or more of*] the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe levels of naturally-occurring substance in environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Is there is a long history of human oral exposure without any reports of immunotoxicological effects (*). AND/OR

No evidence of subchronic oral toxicity effects: A literature search of the [*e.g. TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year range*] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the search words, to ascertain whether there were any *subchronic oral* toxicity data on humans and/or other mammals. There [*are/are no*] *subchronic oral* toxicity data available. [*NOTE: If subchronic oral toxicity effects have been reported, but do not reflect exposure to the active ingredient under conditions of use, give information regarding the subchronic oral toxicity effects, the likelihood of their occurrence under conditions of use, and literature citation(s)*] (*)

Proposed label uses mitigate/eliminate exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating direct exposure to humans, AND/OR timing of application precludes direct/indirect oral exposure to humans [*Discuss proposed label use sites and rate/timing of application, application methods and its effects on limiting subchronic oral exposure*] (*).

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph IX for further guidance)

IX. Subchronic Dermal Toxicity - 90 day (90-day Dermal) (OPPTS 870.3250)

ACTIVE INGREDIENT:

SYNONYMS:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct a 90-day Dermal Toxicity Study (OPPTS 870.3250). The waiver request is based on the rationale that (one or more of the following):

a. The product containing [*active ingredient name*] is not intended for purposeful application to human skin or will not result in comparable prolonged exposure to human skin and: (i) a subchronic oral toxicity study is not required; and (ii) [*active ingredient name*] is not known or expected to be metabolized differently by the dermal route of exposure than by the oral route, and metabolites of the active ingredient are not toxic moieties. AND/OR

b. An extensive literature search yielded no reports of subchronic dermal toxicity effects in [*humans, rodents, other mammals, etc*] from [*active ingredient name*] AND/OR

c. [*Active ingredient name*] is ubiquitous in the environment and and humans are regularly exposed to this substance dermally at levels that are [equal to/greater than] that which would be expected from the product under conditions of use. (*)

d. The proposed uses of [*product name*] on [*use sites/crops*] will not result dermal exposure to humans under conditions of use [*Discuss how/why*]. Therefore, testing is not considered necessary to assess the potential subchronic dermal toxicity of [*active ingredient name*]. AND/OR

d. The product containing [a*ctive ingredient name*] is contained within a trap or closed dispenser that precludes any dermal exposure to workers, applicators, and/or the public.

e. The TGAI and/or product is corrosive or has a pH <2.0 or >11.5. The pH is [*too low/too high*] to conduct these studies

WAIVER REQUEST JUSTIFICATION:
The waiver request for an subchronic dermal toxicity – 90 day study is based on [*one or more of*] the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe levels of naturally-occurring substance in

environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Is there is a long history of human dermal exposure without any reports of subchronic dermal effects (*). AND/OR

No evidence of subchronic dermal toxicity effects: A literature search of the [*e.g. TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year range*] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the search words, to ascertain whether there were any subchronic dermal toxicity data on humans and/or other mammals. There [*are/are no*] subchronic dermal toxicity data available. [*NOTE: If subchronic dermal toxicity effects have been reported, but do not reflect exposure to the active ingredient under conditions of use, give information regarding the subchronic oral toxicity effects, the likelihood of their occurrence under conditions of use, and literature citation(s)*] (*)

Proposed label uses mitigate/eliminate exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating direct and repeated dermal exposure to humans, AND/OR timing of application precludes direct/indirect repeated dermal exposure to humans [*Discuss proposed label use sites and rate/timing of application, application methods and its effects on limiting subchronic dermal exposure*] (*).

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph IX for further guidance)

X. Subchronic Inhalation Toxicity (90-day Inhalation) (OPPTS 870.3465)

ACTIVE INGREDIENT:

SYNONYMS:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct a 90-day Inhalation Toxicity Study (OPPTS 870.3465). The waiver request is based on the rationale that (one or more of the following):

a. The product containing [*active ingredient name*] will not result in repeated inhalation exposure at a concentration that is likely to be toxic. AND/OR

b. An extensive literature search yielded no reports of subchronic inhalation toxicity effects in [*humans, rodents, other mammals, etc*] from inhalatio exposure to [*active ingredient name*] AND/OR

c. [*Active ingredient name*] is ubiquitous in the environment and and humans are regularly exposed to this substance via inhalation at levels that are [equal to/greater than] that which would be expected from the product under conditions of use. (*)

d. The proposed uses of [*product name*] on [*use sites/crops*] will not result inhalation exposure to humans under conditions of use [*Discuss how/why*]. Therefore, testing is not considered necessary to assess the potential subchronic inhalation toxicity of [*active ingredient name*]. AND/OR

d. The product containing [a*ctive ingredient name*] is contained within a trap or closed dispenser that precludes any inhalation exposure to workers, applicators, and/or the public.

e. The TGAI and/or product is corrosive or has a pH <2.0 or >11.5. The pH is [*too low/too high*] to conduct these studies

WAIVER REQUEST JUSTIFICATION:

The waiver request for an subchronic inhalation toxicity study is based on [*one or more of*] the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe levels of naturally-occurring substance in environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Is there is a long history of human inhalation exposure without any reports of subchronic inhalation effects (*). AND/OR

No evidence of subchronic inhalation toxicity effects: A literature search of the [*e.g. TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year range*] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the search words, to ascertain whether there were any subchronic inhalation toxicity data on humans and/or other mammals. There [*are/are no*] subchronic inhalation toxicity data available. [*NOTE: If subchronic inhalation toxicity effects have been reported, but do not reflect exposure to the active ingredient under conditions of use, give information regarding the subchronic inhalation toxicity effects, the likelihood of their occurrence under conditions of use, and literature citation(s)*] (*)

Proposed label uses mitigate/eliminate exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating direct and repeated inhalation exposure to humans, AND/OR timing of application precludes direct/indirect repeated inhalation exposure

to humans [*Discuss proposed label use sites and rate/timing of application, application methods and its effects on limiting subchronic dermal exposure*] (*).

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph IX for further guidance)

XI. Preliminary Developmental Toxicity Screen (Teratogenicity) (OPPTS 870.3500)

ACTIVE INGREDIENT:

SYNONYMS:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct a Preliminary Developmental Toxicity Study (OPPTS 870.3500). The waiver request is based on the rationale that (one or more of the following):

a. Use of the product containing [active ingredient] under widespread and recognized practice, is not reasonably expected to result in significant exposure to female humans [*Discuss how/why*], AND its use does not require a tolerance or an exemption from the requirement of a tolerance, or ists use requires a food additive regulation. AND/OR

b. An extensive literature search yielded no reports of teratogenicity in [*humans, rodents, other mammals, etc*] from inhalatio exposure to [*active ingredient name*] AND/OR

c. [*Active ingredient name*] is ubiquitous in the environment and and humans are regularly exposed to this substance via [*describe routes of exposure*] at levels that are [equal to/greater than] that which would be expected from the product under conditions of use. (*)

d. The proposed uses of [*product name*] on [*use sites/crops*] will not result exposure to humans under conditions of use [*Discuss how/why*]. Therefore, testing is not considered necessary to assess the potential teratogenicity of [*active ingredient name*]. AND/OR

d. The product containing [a*ctive ingredient name*] is contained within a trap or closed dispenser that precludes any exposure to workers, applicators, and/or the public.

e. The TGAI and/or product is corrosive or has a pH <2.0 or >11.5. The pH is [*too low/too high*] to conduct these studies

WAIVER REQUEST JUSTIFICATION:
The waiver request for a teratogenicity study is based on [*one or more of*] the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe levels of naturally-occurring substance in environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Is there is a long history of human exposure without any reports of teratogenicity (*). AND/OR

No evidence of teratogenicity: A literature search of the [*e.g. TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year range*] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the search words, to ascertain whether there were any teratogenicity data on humans and/or other mammals. There [*are/are no*] teratogenicity data available. [*NOTE: If teratogenicity has been reported, but does not reflect exposure to the active ingredient under conditions of use, give information regarding the teratogenic effects, the likelihood of their occurrence under conditions of use, and literature citation(s)*] (*)

Proposed label uses mitigate/eliminate exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating exposure to humans, AND/OR timing of application precludes direct/indirect exposure to humans [*Discuss proposed label use sites and rate/timing of application, application methods and its effects on limiting subchronic dermal exposure*] (*).

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph IX for further guidance)

Sample Waiver Request Format For Biochemical Pesticide Non-Target Organism Data Requirements

To determine that a waiver request conforms to the guidance listed in the Overview, the following information must be submitted on a Guideline-by-Guideline basis:

STUDY TYPES: **Tier I:**

[see also:
Special Considerations for Conducting Aquatic Laboratory Studies (OPPTS 850.1000);
and
Background - Nontarget Plant Testing (OPPTS 850.4000)]

I. Avian Acute Oral Toxicity (OPPTS 850.2100) and Avian Dietary Toxicity (OPPTS 850.2200)

ACTIVE INGREDIENT:

SYNONYMS:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct Avian Acute Oral Toxicity studies (OPPTS 850.2100) and Avian Dietary Toxicity studies (OPPTS 850.2200) The waiver request is based on the rationale that (one or more of the following):

a. [*active ingredient name*] is a naturally-occurring substance [*describe source*], whose level in the environment will not significantly increase above background levels and/or will rapidly degrade when [*product name*] is used in accordance with proposed label use directions. AND/OR

b. An extensive literature search yielded no reports of toxicity or other adverse effects in birds on an acute and/or dietary basis. AND/OR

c. The proposed uses of [*product name*] on [*use sites/crops*] will not result in any exposure or adverse effects to birds [*Discuss how/why*]. Therefore, testing is not considered necessary to assess the risks of [*active ingredient name*] to avian wildlife.

WAIVER REQUEST JUSTIFICATION:
The waiver request is based on the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe levels of naturally-occurring substance in environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Describe environmental fate and/or degradation rate and/or formation of metabolites and metabolite fate/degradation (*). AND/OR

No evidence of toxicity and/or adverse effects: A literature search of the [*e.g. AGRICOLA, TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year range*] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the search words, to ascertain whether there were any acute and dietary toxicity data on birds. The search was also used to ascertain if there were any genotoxic, carcinogenic, allergenic, mutagenic, and teratogenic data on birds exposed to [*active ingredient name*]. There [*are/are no*] data available demonstrating that there are [*toxic effects/no toxic effects*] on birds exposed to naturally-occurring sources of [*active ingredient name*] (*)

Proposed label uses mitigate/eliminate exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating direct exposure to birds, AND/OR Timing of application precludes direct/indirect exposure to birds [*Discuss proposed label use sites and rate/timing of application, application methods and its effects on limiting drift/runoff, if applicable*], AND/OR give degradation rates of active ingredient in days/weeks/months, if available(*).

Would runoff or overspray result in effects not seen from the naturally occurring AI levels?.

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph X for further guidance)

II. **Fish Acute Toxicity Test, Freshwater and Marine (OPPTS 850.1075)**
Aquatic Acute Toxicity Test, Freshwater Daphnids (OPPTS 850.1010)
Mysid Acute Toxicity Test (OPPTS 850.1035; if marine environments are potentially exposed)

ACTIVE INGREDIENT:

SYNONYMS:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct Fish Acute Toxicity studies (OPPTS 850.1075) and Aquatic Acute Toxicity, Freshwater Daphnids, studies (OPPTS 850.1010) and (if applicable) Mysid Acute Toxicity studies (OPPTS 850.1035) The waiver request is based on the rationale that (one or more of the following):

a. [*active ingredient name*] is a naturally-occurring substance [*describe source*], whose level in the environment will not significantly increase above background levels and/or will rapidly degrade when [*product name*] is used in accordance with proposed label use directions. AND/OR

b. An extensive literature search yielded no reports of toxicity or other adverse effects in fish, and/or aquatic invertebrates. AND/OR

c. The proposed uses of [*product name*] on [*use sites/crops*] will not result in any exposure or adverse effects to fish and/or aquatic invertebrates via direct application, and/or spray drift, and/or runoff [*Discuss how/why*]. Therefore, testing is not considered necessary to assess the risks of [*active ingredient name*] to aquatic organisms.

WAIVER REQUEST JUSTIFICATION:
The waiver request is based on the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe levels of naturally-occurring substance in environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Describe environmental fate and/or degradation rate and/or formation of metabolites and metabolite fate/degradation (*). AND/OR

No evidence of toxicity and/or adverse effects: A literature search of the [*e.g. AGRICOLA, TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year range*] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the search words, to ascertain whether there were any toxicity data on fish and aquatic invertebrates. The search was

also used to ascertain if there were any genotoxic, carcinogenic, allergenic, mutagenic, and teratogenic data on fish and aquatic invertebrates exposed to [*active ingredient name*]. There [*are/are no*] data available demonstrating that there are [*toxic effects/no toxic effects*] on fish and aquatic invertebrates exposed to naturally-occurring sources of [*active ingredient name*] (*)

Proposed label uses mitigate/eliminate exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating direct exposure to fish and aquatic invertebrates, AND/OR Timing of application precludes direct/indirect exposure to fish and aquatic invertebrates [*Discuss proposed label use sites and rate/timing of application, application methods and its effects on limiting drift/runoff, if applicable*], AND/OR give degradation rates of active ingredient in days/weeks/months, if available(*).

Would runoff or overspray result in effects not seen from the naturally occurring AI levels?.

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph X for further guidance)

III. Nontarget Plant Studies
Target Area Toxicity (OPPTS 850.4025)
Terrestrial plant toxicity, Tier I (Seedling emergence) (OPPTS 850.4100)
Terrestrial plant toxicity, Tier I (Vegetative vigor) (OPPTS 850.4150)
Seedling Germination/root elongation toxicity test (OPPTS 850.4200)
Aquatic Plant Toxicity Test Using Lemna spp. (Tiers I and II) (OPPTS 850.4400)

ACTIVE INGREDIENT:

SYNONYMS:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct Terrestrial and/or Aquatic Plant Toxicity Studies (OPPTS 850.4100; 850.4150; 850.4200; & 850.4400) The waiver request is based on the rationale that (one or more of the following):

a. [*active ingredient name*] is a naturally-occurring substance [*describe source*], whose level in the environment will not significantly increase above background levels and/or will rapidly degrade when [*product name*] is used in accordance with proposed label use directions. AND/OR

b. An extensive literature search yielded no reports of toxicity or other adverse effects in

terrestrial and/or aquatic plants. AND/OR

c. The proposed uses of [*product name*] on [*use sites/crops*] will not result in any exposure or adverse effects to non-target terrestrial and/or aquatic plants via direct application, and/or spray drift, and/or runoff [*Discuss how/why*]. Therefore, testing is not considered necessary to assess the risks of [*active ingredient name*] to aquatic organisms.

WAIVER REQUEST JUSTIFICATION:
The waiver request is based on the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe levels of naturally-occurring substance in environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Describe environmental fate and/or degradation rate and/or formation of metabolites and metabolite fate/degradation (*). AND/OR

No evidence of toxicity and/or adverse effects: A literature search of the [*e.g. AGRICOLA, TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year range*] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the search words, to ascertain whether there were any toxicity data on fish and aquatic invertebrates. The search was also used to ascertain if there were any genotoxic, carcinogenic, allergenic, mutagenic, and teratogenic data on non-target plants exposed to [*active ingredient name*]. There [*are/are no*] data available demonstrating that there are [*toxic effects/no toxic effects*] on non-target plants exposed to naturally-occurring sources of [*active ingredient name*] (*)

Proposed label uses mitigate/eliminate exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating direct exposure to non-target plants, AND/OR Timing of application precludes direct/indirect exposure to non-target plants [*Discuss proposed label use sites and rate/timing of application, application methods and its effects on limiting drift/runoff, if applicable*], AND/OR give degradation rates of active ingredient in days/weeks/months, if available(*).

Would runoff or overspray result in effects not seen from the naturally occurring AI levels?.

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph X for further guidance)

IV. Nontarget Insect Studies

Honey Bee Contact Toxicity (OPPTS 850.3020)
Honey Bee Toxicity of Residues on Foliage (OPPTS 850.3030)
Field Testing for Pollinators (OPPTS 850.3040)

ACTIVE INGREDIENT:

SYNONYMS:

REQUESTED BY:

SUMMARY (EXAMPLE): [*Registrant Name/Company*] requests waivers from the requirement to conduct non-target insect studies (OPPTS 850.3020; and/or 850.3030; and/or 850.3040). The waiver request is based on the rationale that (one or more of the following):

a. [*active ingredient name*] is a naturally-occurring substance [*describe source*], whose level in the environment will not significantly increase above background levels and/or will rapidly degrade when [*product name*] is used in accordance with proposed label use directions. AND/OR

b. An extensive literature search yielded no reports of toxicity or other adverse effects in non-target insects. AND/OR

c. The proposed uses of [*product name*] on [*use sites/crops*] will not result in any exposure or adverse effects to non-target terrestrial and/or aquatic insects via direct application, and/or spray drift, and/or runoff [*Discuss how/why*]. Therefore, testing is not considered necessary to assess the risks of [*active ingredient name*] to non-target insects.

WAIVER REQUEST JUSTIFICATION:
The waiver request is based on the following rationales:

Increased environmental exposure to [*active ingredient name*], due to use of the end-use product, [*product name*], will be minimal: Describe levels of naturally-occurring substance in environment/use site (*). Is it ubiquitous in nature [*give geographical distribution and sources**]; has it been isolated from [*soil?, plants/, crops/vegetables/fruits? insects/, streams?, ponds?, lakes?**]. Describe environmental fate and/or degradation rate and/or formation of metabolites and metabolite fate/degradation (*). AND/OR

No evidence of toxicity and/or adverse effects: A literature search of the [*e.g. AGRICOLA, TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX (Hazardous and Regulated Chemicals Database), (or OTHER)**] databases for the period [*year range*] was conducted using [*active ingredient name*], it's synonyms (if any), and metabolites (if any), as the search words, to

ascertain whether there were any toxicity data on insects. The search was also used to ascertain if there were any genotoxic, carcinogenic, allergenic, mutagenic, and teratogenic data on non-target insects exposed to [*active ingredient name*]. There [*are/are no*] data available demonstrating that there are [*toxic effects/no toxic effects*] on non-target insects exposed to naturally-occurring sources of [*active ingredient name*] (*)

Proposed label uses mitigate/eliminate exposure: Use of [*product name*] will be limited to [*soil, seed, foliar, greenhouse , etc*] applications [*by spray, dip, soil incorporation, aerial, etc.*] on [*crops/use sites*], thus minimizing/eliminating direct exposure to non-target insects, AND/OR Timing of application precludes direct/indirect exposure to non-target plants [*Discuss proposed label use sites and rate/timing of application, application methods and its effects on limiting drift/runoff, if applicable*], AND/OR give degradation rates of active ingredient in days/weeks/months, if available(*).

Would runoff or overspray result in effects not seen from the naturally occurring AI levels?.

* **References Cited:** references should numbered (1, 2, 3, etc.) and listed in this section, and be listed in text as if in a published technical journal article (see also Overview paragraph X for further guidance)